Exhibit H

MEMORANDUM

DATE:	December 2, 1996
FROM:	Veronica Price Biomedical Engineer ODE/DCRND/ICDG
TO:	The Record
RE:	Reclassification of Cardiovascular Intravascular Filters

Introduction:

This memo has been prepared in accordance with the ODE Guidance on Reclassification of Devices for Reviewers. The goal of this memo is to review the regulatory history of the cardiovascular intravascular filter, provide detail on the known risks associated with this device and justify the down classification from class III to class II. (Note: This reclassification is not intended to cover the Bird's Nest Filter marketed by Cook under P850049. The device description has been written such that it precludes this particular filter design.)

Regulatory History of Device:

(I) Proposed for class III (Three) by Cardiovascular Device Classification Panel March 9, 1979 (44 FR 13284).

The Reclassification Panel cited the following reasons for recommending Class III classification for this device:

- The device is an implant used for life sustaining purpose;
- The materials used in the device and its design should minimize the thromboembolic complications;
- The materials used in the device and its design should minimize the tendency to perforate the vena cava; and
- The device should allow as much venous blood to return to the heart as possible.

(ii) Final Rule promulgated February 5, 1980 (45 FR 17736), classifying Cardiovascular Intravascular Filters (21 CFR 870.3375) as Class III devices.

An amendment to the final rule was published May 11, 1987 (52 FR 17736) stating that a date for PMA or PDP requirement would be published.

(iii) a. Federal Register Notice of August 14, 1995, (60FR41986), requiring manufacturers of 31 group 2, Class III devices to submit to FDA summaries of, and citations to, safety and effectiveness information known for these devices.

b. Reclassification submissions received from Nitinol Medical Technologies on July 22, 1996, and B. Braun Vena Tech on September 30, 1996.

C. 515(I) submission received from Boston Scientific Corporation on August 14, 1996.

This reclassification has been initiated by the two manufacturers cited above (b.).

Device Description:

A cardiovascular intravascular filter is an permanent implant that is placed in the inferior vena cava for the purpose of preventing pulmonary thromboemboli (blood clots generated in the lower limbs and broken loose into the blood stream) from flowing into the right side of the heart and the pulmonary circulation. The filter is seated within the vena cava via a series of hooks which are at the end of several legs or struts which converge at an apex. The goal of filter placement is to try to obtain high filtering efficiency (large and small emboli) without impedance of blood flow, reduced device related thrombosis, migration and without penetration of the vessel wall. It is indicated for the prevention of recurrent pulmonary embolism via placement in the vena cava in the following situations: pulmonary thromboembolism when anticoagulants are contraindicated; failure of anticoagulant therapy in thromboembolic diseases; emergency treatment following massive pulmonary embolism where anticipated benefits of conventional therapy are reduced; and chronic, recurrent pulmonary embolism where anticoagulant therapy has failed or is contraindicated.

Proposed Reclassification:

A. Identification

Cardiovascular Intravascular Filter

B. Recommended Classification

Class II
Special Controls: Standard Labeling (Intended Use)
Device Guideline

C. Risks to Health

When the cardiovascular intravascular filter was proposed for classification into class III, (44 FR 13284), the panel provided reasons for their recommendation. The reasons included the risk of: thromboembolism, vena cava perforation, and decreased blood flow to the right heart (caval occlusion). Following FDA's review of the reclassification petitions, 515(I) submission, MDR's and the literature, additional risks have been identified. They include: complications during filter insertion; death; thrombogenicity;

filter migration; filter tilting and angulation; filter embolization; and fracture of filter. Although these risks are potentially life threatening, as is the disease they are intended to treat, they are well known to the users and are well characterized in the medical literature. FDA now believes that these risks can be controlled by special controls.

On the basis of its review, FDA now believes that the use of the cardiovascular intravascular filter for the prevention of recurrent pulmonary embolism via placement in the vena cava in the following situations: pulmonary thromboembolism when anticoagulants are contraindicated; failure of anticoagulant therapy in thromboembolic diseases; emergency treatment following massive pulmonary embolism where anticipated benefits of conventional therapy are reduced; and chronic, recurrent pulmonary embolism where anticoagulant therapy has failed or is contraindicated, does not present a potential unreasonable risk of illness and injury, and that special controls would provide reasonable assurance of the safety and effectiveness of the device. The published guideline and standard labeling are special controls for this device.

D. Summary of reasons for reclassification

FDA has determined that the following reasons support its recommendation to reclassify the cardiovascular intravascular filter from class III to class II:

1. General controls by themselves are insufficient to provide reasonable assurances of the safety and effectiveness of the device.

2. There is sufficient publicly available information to establish special controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use.

3. There is sufficient publicly available information to demonstrate that the risks to health have been characterized for the cardiovascular intravascular filter and that the relationships between the performance characteristics and these risks have been established.

Cardiovascular Intravascular Filters can be reclassified from Class III to Class II because it meets the criteria of 513(e) (2) of the act. Special controls in the form of standardized labeling and a device guidelines on vena cava filters have been developed. These special controls, in addition to general controls, provide reasonable assurance of the safety and effectiveness of the device, and there is sufficient information to establish special controls to provide such assurance. A regulatory level of Class III is unnecessary.

E. Summary of data upon which the reclassification is based

A recommendation to down classify cardiovascular intravascular filters (870.3375) from Class III to Class II is being proposed. This recommendation is based on an extensive review of published reports concerning this category of devices, information submitted in reclassification petitions and by manufacturers in response to the published 515(I), a review of MDR's, and previously cleared 510(k)'s.

Cardiovascular intravascular filters have a long history of use. Over the course of this time, the potential benefits and risks have been well characterized. It is possible and appropriate to minimize the risks through the use of special controls. These controls include standardized labeling as well as published guidelines.

The labeling that has been developed for marketed filters includes a list of approved indications for use. A required contraindication is identified and a warning statement regarding MRI compatibility are all mandated. Additional contraindications and warnings may be added to address particular device issues.

Although there are no existing published guidelines or guidance documents for this category of devices, the review of previously submitted 510(k)'s and IDE's has demonstrated a set of consistent requirements in terms of required data. A formal guideline is being developed concurrently with the review of the information on reclassification. The guidance document will help to convey to manufacturers of these products the necessary in vitro, animal and human clinical data that will be necessary to support marketing clearance.

Known Risks:

A. Complications during filter insertion

The filter is delivered using several different components of a system which include a sheath, guidewire, and introducer. The overall insertion success rate is usually about 95% but there may be difficulties in correctly placing the filter in up to 15% (Ref. 7). In the course of trying to place the filter in the vena cava the following complications have been noted: sheath perforation; introducer tip detachment; guidewire kinking; and sheath kinking (Refs. 6 and 16). These complications can result in filter deformation; fracture; premature release or insufficient opening; improper placement; and thrombus formation on filter which may result in insufficient opening (Ref. 7). There have also been reports of problems with the filter sticking to and/or getting caught in the introducer while the device is being deployed, practitioner difficulty with inserting and/or retrieving failed insertions of the device, and problems with the filter legs breaking during insertion and deployment within the introducer and/or breakage of the filter /filter legs upon placement of the device within the patient (Ref. 4). These complications are a function of the design of the delivery system, the adherence to the instructions for use and human error. The risks can be controlled by special controls.

B. Recurrent Pulmonary Embolism

The incidence of PE reported in the literature is 1.9% to 5% (Refs. 11, 17, and 22) despite the presence of a filtering device. Mortality from PE with a filter in place is 0.9%. (Ref. 17) Medical opinion is that the risk of PE from untreated proximal DVT is as high as 50% and that PE mortality without treatment is 8% (Refs. 5 and 13). Such recurrences almost always occur within the first three months, usually within one month (Ref. 11). Some of the mechanisms which may be responsible for PE after filter insertion are the following: ineffective filtration; continuous growth of trapped thrombi through the filter; development of thrombosis on the proximal end of the filter; filter migration to a position where it does not function optimally; filter retraction from the caval wall at thrombus retention, occurring if some of the hooks have grasped the thrombus, which creates a channel between the filter and the caval wall; and embolization through collaterals that may be lumbar or embolization that may be via the ovarian/spermatic veins; embolization from thrombi proximal to the filter (arm veins, renal or hepatic veins, the right heart); and incorrect position of the filter (Ref. 7). The risk of recurrent PE is a function of material selection, device design and adherence to the instructions for use and can be controlled by special controls.

c. Death

The death rate associated with filter use that can be attributed to filter complications is low and has been reported to be from 0.12% to 4% (Refs. 14 and 17). Death attributable to filter complications have been reported to result from cardiac arrest immediately following filter placement, misplacement of the filter during insertion and cephalic migration of a filter to the heart after placement. This risk can be attributed to user error or design flaws. This risk of death can be controlled by special controls.

D. Thrombogenicity

The materials of the device should be biocompatible and not lead to thrombogenicity. The affect on the blood flow should not be great enough to cause stasis which would lead to thrombus formation in and around the device. Reported rates of IVC thrombus vary from 7 to 22% (Refs. 7 and 12). The proper choice of materials and the design of the device to minimize or eliminate the risk of stasis can be controlled by special controls.

E. Filter Migration

The design of the filter must be such that it is stable within the vena cava. The filter release mechanism that is part of the delivery system must be simple and controlled such that the filter is deployed in the desired location and is completely opened. If it is not, it

can ultimately propagate into the right heart or it may tilt such that its filtering efficiency is compromised. The occurrence of filter migration in the literature varies from 6% to 53% (Refs. 8, 9, 18, and 23). Minor filter migration in the caudal or cephalic direction is commonly reported and does not appear to be associated with clinically significant events. Much of the reported filter movement may actually be due to measurement error resulting from differences in patient positioning, breathing and parallax. True migration may be caused by too large a vena cava, inadequate positioning and massive embolization into the filter with caval dilatation (Ref. 7). The risk of migration can be controlled by special controls.

F. Caval Penetration

The filter must be designed such that it is secure within the vena cava without penetrating the wall of this vessel and potentially penetrating nearby organs. Slight penetration of the caval wall by filter struts is usually asymptomatic and clinically insignificant perhaps because penetration occurs gradually, allowing time for the vessel wall to fibrose. A caval penetration rate of 9% has been reported (Ref. 12). There have been rare cases, however, when strut migration or breakage have led to retroperitoneal complications such as bowel perforation, neurovascular injury or small bowel obstruction. This risk may be controlled by special controls.

G. Filter Tilting and Angulation

The significance of tilting and angulation of caval filter after placement is controversial. There is a theoretical loss of filtering efficacy of any filter when tilted or angulated significantly; however there is no good clinical data to support a definite increased incidence in PE or failure to trap thrombi. A properly designed device should minimize the possibility for tilting upon deployment or angulating after implantation. This risk can be controlled by special controls.

H. Caval Occlusion

Caval occlusion is related to filter thrombogenicity, design and flow patterns (Ref. 7). Small or moderate sized emboli trapped in a filter are usually asymptomatic since the residual patency of the vena cava and the normal paravertebral collateral veins permit adequate venous return. A large trapped embolus or a cluster of small emboli may occlude a filter completely and thus block the vena cava. After a period of days or weeks, the occlusion occurs and causes a sudden swelling of both lower limbs. In almost all cases the symptoms of IVC occlusion are transient and resolve almost completely within a few weeks or a few months since the thrombi undergo spontaneous lysis. It is often clinically difficult or impossible to distinguish IVC filter occlusion from extension of the preexisting DVT, since the symptoms may be similar. Optimally, the filter should capture all clinically threatening PE above a critical size. Rates of occlusion for the various filters has been reported to be anywhere from 4% to 18% (Refs. 15 and 24). This complication is a function of device design and is clinically manageable under most

circumstances. The risk of caval occlusion can be controlled by special controls.

I. Filter Embolization

The risk of filter embolization is primarily limited to the first two weeks after implantation. After two weeks, the points of contact between the device and the vein wall become tightly bound by collagen, muscle fibers and neoendothelium and embolization of the filter becomes virtually impossible. Embolization of the filter is a serious complication with variable clinical consequences, comparable to pulmonary thromboembolism. These range from being totally asymptomatic to sudden death. Therapy also ranges from no therapy to open chest surgery and removal of the device. Proper design and close adherence to the instructions for use can minimize the risk of filter embolization. This risk can be controlled by special controls.

J. Fracture of filter

Filters may fracture as a result of direct trauma to the abdomen, or from a metal fatigue phenomenon when perforation exists and the tip of the leg becomes locked into a vertebral body or adjacent immobile tissues whereby respiratory motion may then cause repeated unanticipated flexion of the filter leg, or it may fracture due to metal corrosion and weld. The fracture fragments may migrate locally or distally. This complication usually is asymptomatic and requires no treatment. The incidence of occurrence has been reported at 2% (Ref. 12). Filter fracture is a function of design and delivery into the IVC. The risk can be controlled by special controls.

K. Other Risks

The complications that occur at the puncture site are not uniquely related to delivery of intravascular cardiovascular filters but represent the complications observed with various catheter techniques. Events occurring at the delivery site include: hematoma formation and A-V fistula, DVT at puncture site, pneumothorax and air embolism after jugular insertion. Many of these events can be minimized or eliminated by appropriate operator training and comprehensive device labeling. Most are well known risks associated with many different interventional procedures which can be controlled by special controls.

L. **Benefits**

Pulmonary embolism is a serious clinical issue causing significant morbidity and mortality. It has been estimated that there are more than 600,000 cases of clinically significant PE occur each year in the United States (Refs. 10 and 25), resulting in approximately 200,000 deaths annually in the United States (Ref. 21). The patient often survives the first embolism but is at high risk that a second fatal PE will occur. PE recurs in approximately 6 to 25% of treated patients (Ref. 25). Additionally, the incidence of PE

in patients with DVT is 19% to 28% (Ref. 20). Treatment of PE has been shown to be effective in reducing the mortality from 30% to 8% (Ref. 10). Normally, patients with deep venous thrombosis and/or PE are treated with anticoagulation therapy. However, in some patients anticoagulation is ineffective, contraindicated or results in complications which require that it be discontinued. For these patients, vena caval interruption is recommended. Historically, vena cava interruption was achieved first by ligation which involved the direct suturing of the IVC and then by plication with clips around the exterior of the vein. The original concept of surgically ligating the vena cava to prevent PE proved effective but required major surgery and was complicated by significant mortality and venous stasis complications. Also, large collateral venous channels developed, which are capable of allowing the passage of emboli. Suture plication to subdivide the lumen of the vena cava was effective in arresting emboli and had fewer stasis problems, but it still required abdominal surgery. Vena cava filters were then developed. Although placement of filters are not without risks, the likelihood of risks occurring is relatively small and special controls will further minimize these occurrences.

Conclusion:

In summary, FDA believes that based on publicly available, valid scientific evidence, the intravascular cardiovascular filter can be regulated as a Class II device (general and special controls) to reasonably assure that the device is safe and effective for its intended use.

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Veronica A. Price